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510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. The assigned 510(k) number is K140248.

807.92 (a)(1): Name: Hitachi Chemical Diagnostics, Inc.
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Date Prepared: February 19, 2014

807.92 (a)(2): Device name- trade name and common name, and classification

Trade name:
S TEST Reagent Cartridge Carbon Dioxide (CO_2)

Common Name: Routine chemistry analyzer for carbon dioxide

Classification: 21 CFR § 862.1160– Bicarbonate/carbon dioxide test system, Class II, Product Code KHS

807.92 (a)(3): Identification of the legally marketed predicate devices
Carbon Dioxide L3K Assay, Sekisui Diagnostics, PEI, Inc., Canada- K042362

807.92 (a)(4): Device Description
The Hitachi Clinical Analyzer is an automatic, bench-top, wet chemistry system intended for use in clinical laboratories or physician office laboratories. The instrument consists of a desktop analyzer unit, an operations screen that prompts the user for operation input and displays data, a printer, and a unit cover. The analyzer unit includes a single probe, an incubation rotor, carousels for sample cups and reagent cartridges, and a multi-wavelength photometer. The single-use reagent cartridges may be placed in any configuration on the carousel, allowing the user to develop any test panel where the reagent cartridges are available.

The S TEST reagent cartridges are made of plastic and include two small reservoirs capable of holding two separate reagents (R1 and R2), separated by a reaction cell/photometric cuvette. The cartridges also include a dot code label that contains all chemistry parameters, calibration factors, and other production-related information, e.g., expiration dating. The dimensions of the reagent cartridges are: 13.5 mm (W) × 28 mm (D) × 20.2 mm (H).

System operation: After the sample cup is placed into the carousel, the analyzer pipettes the sample, pipettes the reagent, and mixes (stirs) the sample and reagent together. After the sample and reagent react in the incubator bath, the analyzer measures the absorbance of the sample, and based on the absorbance of the reactions, it calculates the concentration of analyte in the sample. The test system can measure analytes in serum or plasma and results are available in approximately 15 minutes per test. This submission is for Reagent Cartridge Carbon Dioxide.

Chemistry reaction: The carbon dioxide (in the form of bicarbonate HCO_3^-) in the sample reacts with phosphoenolpyruvate (PEP) in the presence of phosphoenolpyruvate carboxylase (PEPC) and magnesium to yield oxaloacetic acid (OAA) and phosphate. In the second reaction, and in the presence of malate dehydrogenase (MDH), the reduced cofactor is oxidized by OAA. The reduced cofactor absorbs strongly at 405 nm, whereas its oxidized form does not. The difference in absorbance between the final reading and the blank, monitored bichromatically at 405 nm/508 nm, is directly proportional to the total carbon dioxide concentration in the sample.

807.92 (a)(5): Intended Use

The S TEST Reagent Cartridge Carbon Dioxide (CO_2) is intended for the quantitative determination of carbon dioxide concentration in serum or lithium heparin plasma using the Hitachi Clinical Analyzer E40. Carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance. The S TEST Reagent Cartridge Carbon Dioxide (CO_2) is intended for use in clinical laboratories or physician office laboratories. For *in vitro* diagnostic use only.

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807.92 (a)(6): Technological Similarities and Differences to the Predicate

The following chart describes similarities and differences between the carbon dioxide test systems.

Characteristic	Hitachi S TEST Systems	PREDICATE
Instrument Platform	Hitachi Clinical Analyzer (originally cleared under K111753)	Olympus/Beckman AU400 (originally cleared under K981743)
Carbon Dioxide	K140248	Sekisui K number- K042362
Device Class, Regulation Code	Class II, 21 CFR 862.1160	Same
Classification Product Code	KHS	Same
Intended Use	Quantitative determination of carbon dioxide	Same
Testing Environment	Physician office or clinical lab	Clinical lab
Test Principle	Carbon dioxide (in the form of bicarbonate HCO_3^-) reacts with phosphoenolpyruvate in the presence of phosphoenolpyruvate carboxylase (and magnesium) to yield oxaloacetic acid (OAA). In the presence of malate dehydrogenase, reduced cofactor is oxidized by OAA. The decrease in the concentration of reduced cofactor is monitored, and is proportional to the carbon dioxide concentration in the sample.	Same
Specimen Type	Human serum or lithium heparin plasma	Same
Reportable Range	5.0 to 40.0 mmol/L	2.9 to 50.0 mmol/L
Detection Wavelength	405/508 nm	405/415 nm
Detection Limit (LoQ)	1.3 mmol/L	2.9 mmol/L
Linearity	1.4 to 44.0 mmol/L	2.9 to 50.0 mmol/L
Precision	%CVs range from 1.9% to 6.0% (POL testing)	%CVs range from 1.1% to 1.7% (from product labeling)

807.92 (b)(1): Brief Description of Nonclinical Data

A series of studies were performed that evaluated the following nonclinical performance characteristics: analytical sensitivity (limits of detection), linearity, 20-day in-house precision, interference testing, in-house method comparison, and matrix s comparison between serum and lithium heparin plasma.

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Analytical Sensitivity (Limit of Detection)
The study followed CLSI EP17-A2 where 60 replicates of the reagent blank and 60 replicates of three low samples were tested. The following results were reported: limit of blank = 0.7 mmol/L; limit of detection = 0.9 mmol/L; the limit of quantitation (LoQ) study evaluated three low level specimens in six runs with three instruments over three days. The LoQ was found to be approximately 4 mmol/L, with %CVs less than 11%.

Linearity
The study followed CLSI EP-6A where 10 serial dilutions, plus the zero standard (n = 11), were assayed in duplicate and the results were averaged. The expected values (x-axis) were compared to the observed values (y-axis). The data showed the following linear regression equation: $y = 0.918x + 0.091$; $r^2=0.9988$. The range of linearity was 1.4 mmol/L to 44.0 mmol/L. The reportable range is 5 to 40 mmol/L.

20-day In-house Precision
The studies followed CLSI EP5-A2, where three levels of serum-based commercial controls were each tested in two runs, twice a day, for 20 days. The results were as follows:

Precision Summaries:
Carbon Dioxide- Low Summary

Carbon Dioxide	Within-Run	Total
Mean (mmol/L)	10.11	10.11
SD (mmol/L)	0.13	0.45
%CV	1.3%	4.4%

Carbon Dioxide- Middle Summary

Carbon Dioxide	Within-Run	Total
Mean (mmol/L)	19.41	19.41
SD (mmol/L)	0.25	0.72
%CV	1.3%	3.7%

Carbon Dioxide- High Summary

Carbon Dioxide	Within-Run	Total
Mean (mmol/L)	33.06	33.06
SD (mmol/L)	0.40	1.22
%CV	1.2%	3.7%

Interference Testing (per CLSI EP7-A2)
The data demonstrated that the carbon dioxide test system was not affected by high levels of the following substances at the levels noted:
Lipemia: no interference up to 1,000 mg/dL Intralipid
Ascorbic acid: no interference up to 50 mg/dL
Hemoglobin: no interference up to 1,000 mg/dL
Unconjugated bilirubin: no interference up to 19.1 mg/dL

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Lack of interference was defined as recoveries between 90% and 110% of the neat value, and assay performance claims were established on the HITACHI Clinical Analyzer by testing two serum pools containing approximately 17 and 30 mmol/L carbon dioxide.

Method Comparison
A total of 96 clinical specimens (including 3 spiked and 3 diluted samples) spanning the dynamic range (5.0 to 40.0 mmol/L) were assayed in singleton and in a blinded fashion by both the Hitachi E40 system and a standard laboratory system. The comparative data were analyzed by Deming regression and are shown below. (CI = confidence interval).

Regression Statistics:

n	r	Slope (95% CI)	y-intercept (95% CI)	X mean	Y mean
96	0.981	1.03 (0.97 to 1.08)	0.98 (-0.17 to 2.12)	22.54 mmol/L	24.07 mmol/L

Matrix Comparison
A study was performed to validate the use of lithium heparin plasma as an alternative to serum for the Hitachi Clinical Analyzer with S TEST Reagent Cartridge Carbon Dioxide. Fifty (50) matched serum/plasma samples (including 2 spiked and 4 diluted samples) that spanned the dynamic range (5.0 to 40.0 mmol/L, serum) were assayed in singleton and the results were compared using linear regression (plasma = y-axis). The performance characteristics were as follows.

N = 50
Range (serum) = 5.4 to 38.6 mmol/L carbon dioxide

	Lithium Heparinized Plasma
Slope (95% CIs)	1.00 (0.94 to 1.05)
y-intercept (95% CIs)	-0.34 (-1.97 to 1.30)
r	0.980

Reference Range
Reference range: 22 – 29 mmol/L [1]
1. Tietz, Fundamentals of Clinical Chemistry, 4th Edition, WB Saunders Company, (1996)

Traceability/Calibration
Each lot of S TEST Reagent Cartridge Carbon Dioxide (CO_2) is calibrated by the manufacturer prior to shipment using material referenced to a standard which is traceable to American Chemical Society (ACS) reagent grade sodium carbonate alkalimetric standard. The 2D code printed on each cartridge provides the analyzer with lot-specific calibration data.

Stability
Real time stability testing is ongoing. Stability testing has been performed to support a shelf life of 6 months at 2-8°C.

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807.92 (b)(2): Brief Description of Clinical Data

Studies for precision and method comparison (accuracy) were performed at three external POL-type sites to evaluate the Hitachi E40 Clinical Analyzer with S TEST Reagent Cartridge Carbon Dioxide in one of its targeted intended use environments, the physician's office laboratory.

For the external site precision study, each site received three blinded serum samples (the Precision Panel, labeled A, B, and C) that were chosen to represent low, middle, and high concentrations of carbon dioxide. Each sample was assayed six times per day for five days, reporting 30 results per level. Precision estimates for total precision were as follows:

Carbon Dioxide (mmol/L)
n = 30 replicates per sample per site

Site	Sample	Mean	Within-run Precision		Total Precision	
			SD (mmol/L)	%CV	SD (mmol/L)	%CV
1	A	8.75	0.16	1.8	0.36	4.1
2	A	7.29	0.33	4.6	0.44	6.0
3	A	8.06	0.23	2.9	0.25	3.1
1	B	15.27	0.35	2.3	0.74	4.8
2	B	15.01	0.23	1.5	0.67	4.4
3	B	16.25	0.27	1.7	0.30	1.9
1	C	29.46	0.51	1.7	0.94	3.2
2	C	29.47	0.81	2.7	1.08	3.7
3	C	31.01	0.58	1.9	1.16	3.7

For the external method comparison studies, a series of 47 serum specimens (including three spiked and four diluted samples) with carbon dioxide values ranging from 5.1 to 36.8 mmol/L, were assayed on the Hitachi E40 Clinical Analyzer at three sites using S TEST Reagent Cartridge Carbon Dioxide (y) and a comparative method as the reference method (x). Deming regression yielded the following results:

POL ACCURACY DATA SUMMARY- Carbon Dioxide (mmol/L)

Site #	n	Range (mmol/L)	Regression Equation	"r"	CI** Slope	CI Intercept
1	47	6.6 to 36.8	y = 0.91x + 1.49	0.984	0.87 to 0.95	0.67 to 2.32
2	45*	5.5 to 34.4	y = 0.92x + 0.56	0.970	0.80 to 1.04	-2.31 to 3.43
3	47	5.1 to 35.5	y = 0.92x + 0.79	0.982	0.87 to 0.97	-0.43 to 2.01

* 2 samples at Site 2 quantitated below to dynamic range (<5 mmol/L) and were excluded from data analysis.
**95% Confidence Interval

Expected Range

22 – 29 mmol/L (Tietz, Fundamentals of Clinical Chemistry, 4th Edition, WB Saunders Company, (1996))

807.92 (b)(3): Conclusions from Nonclinical and Clinical Testing

Nonclinical and clinical testing was performed for the Hitachi Clinical Analyzer E40 with Reagent Cartridge Carbon Dioxide. The test system was shown to be safe and effective for its intended use.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

March 11, 2014

HITACHI CHEMICAL DIAGNOSTICS, INC.
c/o ERIKA AMMIRATI
AMMIRATI REGULATORY CONSULTING
575 SHIRLYNN COURT
LOS ALTOS, CA 94022

Re: K140248
Trade/Device Name: S TEST Reagent Cartridge Carbon Dioxide (CO2)
Regulation Number: 21 CFR 862.1160
Regulation Name: Bicarbonate/carbon dioxide test system
Regulatory Class: II
Product Code: KHS
Dated: January 29, 2014
Received: January 30, 2014

Dear Ms. Ammirati:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement on last page.

510(k) Number *(if known)*
k140248

Device Name
S TEST Reagent Cartridge Carbon Dioxide (CO2)

Indications for Use *(Describe)*

The S TEST Reagent Cartridge Carbon Dioxide (CO2) is intended for the quantitative determination of carbon dioxide concentration in serum or lithium heparin plasma using the HITACHI Clinical Analyzer E40. Carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance. The S TEST Reagent Cartridge Carbon Dioxide (CO2) is intended for use in clinical laboratories or physician office laboratories. For in vitro diagnostic use only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Yung W. Chan -S

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